

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

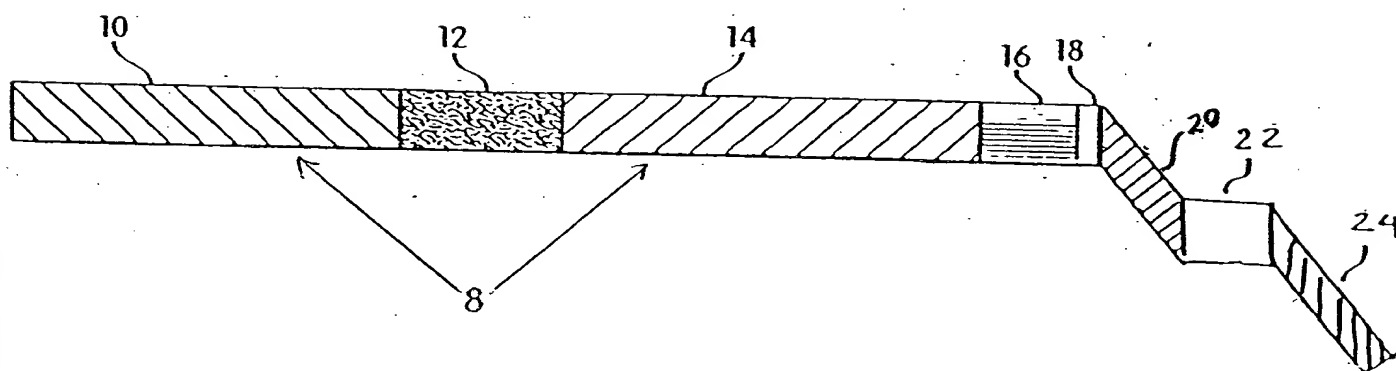
- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

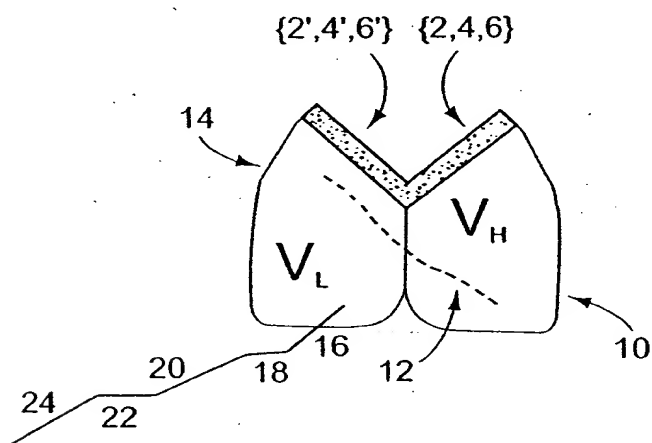
**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

# FIGURE 1

## SINGLE CHAIN BINDING POLYPEPTIDE



(a) Extended Polypeptide

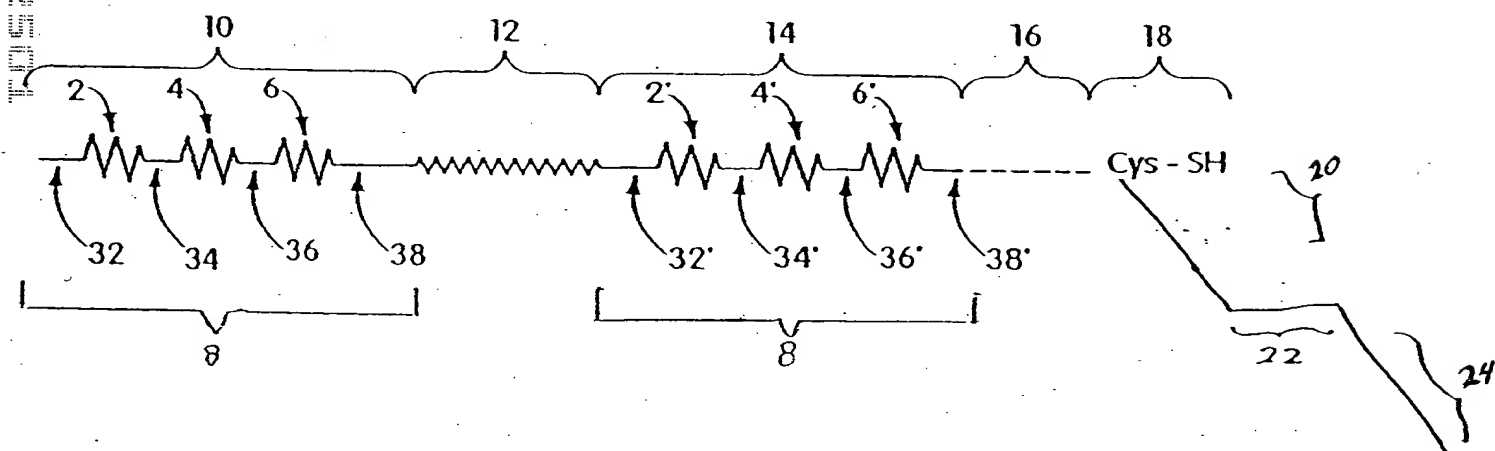


(b) Folded Protein

09888721.002501  
T05290.12/98860

FIGURE 2

SINGLE CHAIN  
BINDING POLYPEPTIDE SHOWING  
LOCATIONS OF COMPLEMENTARITY  
DETERMINING REGIONS, POLYPEPTIDE  
SPACER REGIONS, AND EFFECTOR REGIONS



## FIGURE 3

### C6.5 sFv AMINO ACID SEQUENCE

(N-terminus to C-terminus)

-QVQLQLQSGAE LKKGESLKI SCKGSGYSFT SYWIAWVRQM PGKGLEYMGL  
IYPGDSDTKY SPSFQGQVTI SVDKSVSTAY LQWSSLKPSD SAVYFCARHD  
VGYCSSSNCA KWPEYFQHWG QGTLVTVSSG GGGSGGGGSG  
GGGSQSVLTQ PPSVSAAPGQ KVTISCSGSS SNIGNNYVSW YQQLPGTAPK  
LLIYGHTNRP AGVPDRFSGS KSGTSASLAI SGFRSEDEAD YYCAAWDDSL  
SGWVFGGGTK LTVLG

## FIGURE 4

### C6.5 sFv NUCLEOTIDE SEQUENCE

5'caggtgcagctgttcagctctggggcagagtgaaaaaaccggggagtcctgaagatcctgtaagggttctggataca  
gctttaccagctactggatcgccctgggtgcgccagatgcccggaagcctggagtacatggggctcatctatcctgggtgactc  
tgacaccaaatacagcccgtcctccaaggccaggtcacatctcagtcgacaagtcgagcactgcctacttgcaatggagc  
agtcctgaagccctcggacagcgccgtgtatctgtgcgagacatgacgtgggatattgcagtagttccaactgcgcaaagtggcc  
tgaatactccagcattggggccagggcacccctggtcaccgtctcctcaggtggaggcgggtcaggcggagggtggctctggcg  
gtggcggatcgagctctgtgttgacgcagccgccctcagtgctcggccccaggacagaaggtcacatctcctgctctggaa  
gcagctccaacattgggaataattatgtatcctggtaccagcagctcccaggaacagcccccaactcctcatctatggtcacacca  
atcgggcccgagggtccctgaccgattctctggctccaagctcggcacctcagcctccctggccatcagtggggtccggtccga  
ggatgaggctgattattactgtgcagcatgggatgacagcctgagtggttgggtgttcggcggagggaacagctgaccgtcct  
aggt 3'

# FIGURE 5

## C6ML3-9 sFv' AMINO ACID SEQUENCE

(N-terminus to C-terminus)

-QVQLVQSGAE VKKPGESLKI SCKGSGYSFT SYWIAWVRQM PGKGGLEYMGL  
IYPGDSDTKY SPSFQGQVTI SVDKSVSTAY LQWSSLKPSD SAVYFCARHD  
VGYCSSSNCA KWPEYFQHWG QGTLVTYSSG GGGSGGGGSG  
GGGSQSVLTQ PPSVSAAPGQ KVTISCSGSS SNIGNNYVSW YQQLPGTAPK  
LLIYDHTNRP AGVPDRFSGS KSGTSASLAI SGFRSEDEAD YYCASWDYTL  
SGWVFGGGTK LTVLGAAAH HHHHGGGGC-

# FIGURE 6

## C6ML3-9 sFv' NUCLEOTIDE SEQUENCE

5' caggtgcagctggtgcagtctggggcagaggtgaaaagcccggggagtcctctgaagatcctgtaagggtctggata  
cagctttaccagctactggatcgctgggtgcgccagatgcccgggaaaggcctggagtacatggggctcatctatcctg  
gtgactctgacaccaaatacagccgctcctccaaggccaggtcacatctcagtcgacaagtccgtcagcactgcctac  
ttgcaatggagcagctctgaagccctcggacagcggcgtgtattttgtgcgagacatgacgtgggatattgcagtagttc  
caactgcgcaaagtggcctgaatacttcagcattggggccagggcacccctggteaccgtctcctcaggtggaggcggtt  
caggcggaggtggctctggcgggtggcggatcgagctctgtttgacgcagccgccctcagtgctcgggccccaggacag  
aaggtcacatctcctgctctggaagcagctccaacattgggaataattatgtatcctgggtaccagcagctcccaggaac  
agcccccaaaactcctcatctatgatcacaccaatcgccccgcaggggtccctgaccgattctctggcctcaagtctggca  
cctcagcctccctggccatcagtggttccgggtccgaggtgaggctgattattactgtgcctcctgggactacaccctc  
tcgggctgggtgttcggcggagggaaccaagctgaccgtcctaggtgcggccgcacaccatcatcaccatcacgggtggtg  
cggtgc 3'

# FIGURE 7

## C6ML3-9sFv'-L1-KDEL AMINO ACID SEQUENCE

(N-terminus to C-terminus)

-QVQLVQSGAE VKKPGESLKI SCKGSGYSFT SYWIAWVRQM PGKGLEYMGL  
IYPGDSDTKY SPSFQGQVTI SVDKSVSTAY LQWSSLKPSD SAVYFCARHD  
VGYCSSSNCA KWPEYFQHWG QGTLVTVSSG GGGSGGGGSG  
GGGSQSVLTQ PPSVSAAPGQ KVTISCSGSS SNIGNNYVSW YQQLPGTAPK  
LLIYDHTNRP AGVPDRFSGS KSGTSASLAI SGFRSEDEAD YYCASWDYTL  
SGWVFGGGTK LTVLGAAAH HHHHGGGGCL ESSSSGSEKD EL-

# FIGURE 8

## C6ML3-9 sFv'-L1-KDEL NUCLEOTIDE SEQUENCE

5' caggtgcagctggtgcagtctggggcagaggtgaaaaagcccgaggagtctctgaagatctcctgtaagggttctggata  
cagctttaccagctactggatcgctgggtgcgccagatgcccgggaaaggcctggagtacatggggctcatctatcctg  
gtgactctgacaccaaatacagcccgtcctccaaggccaggtcaccatctcagtcgacaagtccgtcagcactgcctac  
ttgcaatggagcagctcgaagccctcggacagcgccgtgtatfttgtgcgagacatgacgtgggatattgcagtagttc  
caactgcgcaaagtggcctgaatactccagcattggggccagggcaccctggtcaccgtctcctcaggtggaggcggtt  
caggcggaggtggctctggcggtggcggtatcgagctctgtgttgacgcagccgcctcagtgctgcggccccaggacag  
aaggtcaccatctcctgctctggaagcagctccaacattgggaataattatgtatcctggtagcagctcccagggaac  
agcccccaaaactcctcatctatgatcacaccaatcgcccgaggggtccctgaccgattctctggctccaagtctggca  
cctcagcctccctggccatcagtggttccgggtccgaggtgaggtgattattactgtgcctcctgggactacaccctc  
tcgggctgggtgttcggcgagggaaccaagctgaccgtcctaggtgcggccgcacaccatcatcaccatcacggtggtgg  
cggctgcctcgagtcct ctagctctgg atccgaaaaa gatgaactg3'

## FIGURE 9

### C6ML3-9 sFv'-L2-KDEL AMINO ACID SEQUENCE

(N-terminus to C-terminus)

-QVQLVQSGAE VKKPGESLKI SCKGSGYSFT SYWIAWVRQM PGKGLEYMGL  
IYPGDSDTKY SPSFQGQVTI SVDKSVSTAY LQWSSLKPSD SAVYFCARHD  
VGYCSSSNCA KWPEYFQHWG QGTLVTVSSG GGGSGGGGSG  
GGGSQSVLTQ PPSVSAAPGQ KVTISCSGSS SNIGNNYVSW YQQLPGTAPK  
LLIYDHTNRP AGVPDRFSGS KSGTSASLAI SGFRSEDEAD YYCASWDYTL  
SGWVFGGGTK LTVLGAAAH HHHHGGGGCL ESSSSGSSSS GSEKDEL-

## FIGURE 10

### C6ML3-9sFv'-L2-KDEL NUCLEOTIDE SEQUENCE

5' caggtgcagctggtgcagctctggggcagaggtgaaaaagcccggggagtcctgaagatctcctgtaagggttctggata  
cagctttaccagctactggatcgctgggtgcgccagatgccgggaaaggcctggagtacatggggtcatctatcctg  
gtgactctgacaccaaatacagcccgctcctccaaggccaggcaccatctcagtcgacaagtcctcagcactgcctac  
ttgcaatggagcagctctgaagccctcggacagcgccgtgtattttgtgcgagacatgacgtgggatattgcagtagtgc  
caactgcgcaaagtggcctgaatactccagcattggggccagggcaccctggtcaccgtctcctcaggtggaggcggtt  
caggcggaggtggctctggcgggtggcggtatcgagctctgtgtgacgcagccgcccctcagtgctgcggccccaggacag  
aaggcaccatctcctgctctggaagcagctccaacattgggaataattatgtatcctggtaggcagctcccaggaac  
agccccaaactcctcatctatgatcacaccaatcgccccgaggggtccctgaccgattctctggctccaagtctggca  
cctcagcctccctggccatcagtggttccgggtccgaggatgaggctgattattactgtgcctcctgggactacacctc  
tcgggctgggtgttcggcgagggaaccaagctgaccgtcctaggtgcggccgcacaccatcatcaccatcacgggtggtgg  
cggctgcctcgagtcta gcagctccgg ttctctagc tctggatccg aaaaagatga actg 3'

# FIGURE 11

## C6ML3-9 sFv'-L2-H14 AMINO ACID SEQUENCE

(N-terminus to C-terminus)

-QVQLVQSGAE VKKPGESLKI SCKGSGYSFT SYWIAWVRQM PGKGGLEYMG  
IYPGDSDTKY SPSFQGQVTI SVDKSVSTAY LQWSSLKPSD SAVYFCARHD  
VGYCSSNCA KWPEYFQHWG QGTLVTVSSG GGGSGGGGSG  
GGGSQSVLTQ PPSVSAAPGQ KVTISCSGSS SNIGNNYVSW YQQLPGTAPK  
LLIYDHTNRP AGVPDRFSGS KSGTSASLAI SGFRSEDEAD YYCASWDYTL  
SGWVFGGGTK LTVLGAAAH HHHHGGGGCL ESSSSGSSSS  
GSKKSAKKTP KKAKKP-

# FIGURE 12

## C6ML3-9 sFv' -L2-H14 NUCLEOTIDE SEQUENCE

5' caggtgcagctggtgcagctctggggcagaggtgaaaaagcccggggagtcctgaagatctcctgtaagggttctggata  
cagctttaccagctactggatcgccctgggtgcgccagatgcccgggaaaggcctggagtacatggggctcatctatcctg  
gtgactctgacaccaaatacagcccgtccttccaaggccaggtcaccatctcagtcgacaagtcgctcagcactgcctac  
ttgcaatggagcagctctgaagccctcggacagcgccgtgtatgttgcgagacatgacgtgggatattgcagtagttc  
caactgcgcaaagtggcctgaatacttccagcattggggccagggcaccctggtcaccgtctcctcaggtggaggcgggt  
caggcggagggtggctctggcggtggcggtatcgagtcgtgttgacgcagccgcccctcagtgctcgggccccaggacag  
aaggtcaccatctcctgctctggaagcagctccaacattgggaataattatgtatcctggtaccagcagctcccaggaa  
agccccaaactcctcatctatgatcacaccaatcgggccgcaggggtccctgaccgattctctggctccaagtctggca  
cctcagcctccctggccatcagtggttccgggtccgaggatgaggctgattattactgtgcctcctgggactacaccctc  
tcgggctgggtgttcggcgagggaaccaagctgaccgtcctaggtgcggccgcacaccatcatcaccatcacgggtggtg  
cggtgc ctcgagtcta gcagctccgg ttcctctagc tctggatcca agaaaagcgc gaaaaagacc ccgaagaaag  
cgaagaaacc g 3'



## FIGURE 13

### C6ML3-9sFv'-L2-nls AMINO ACID SEQUENCE

(N-terminus to C-terminus)

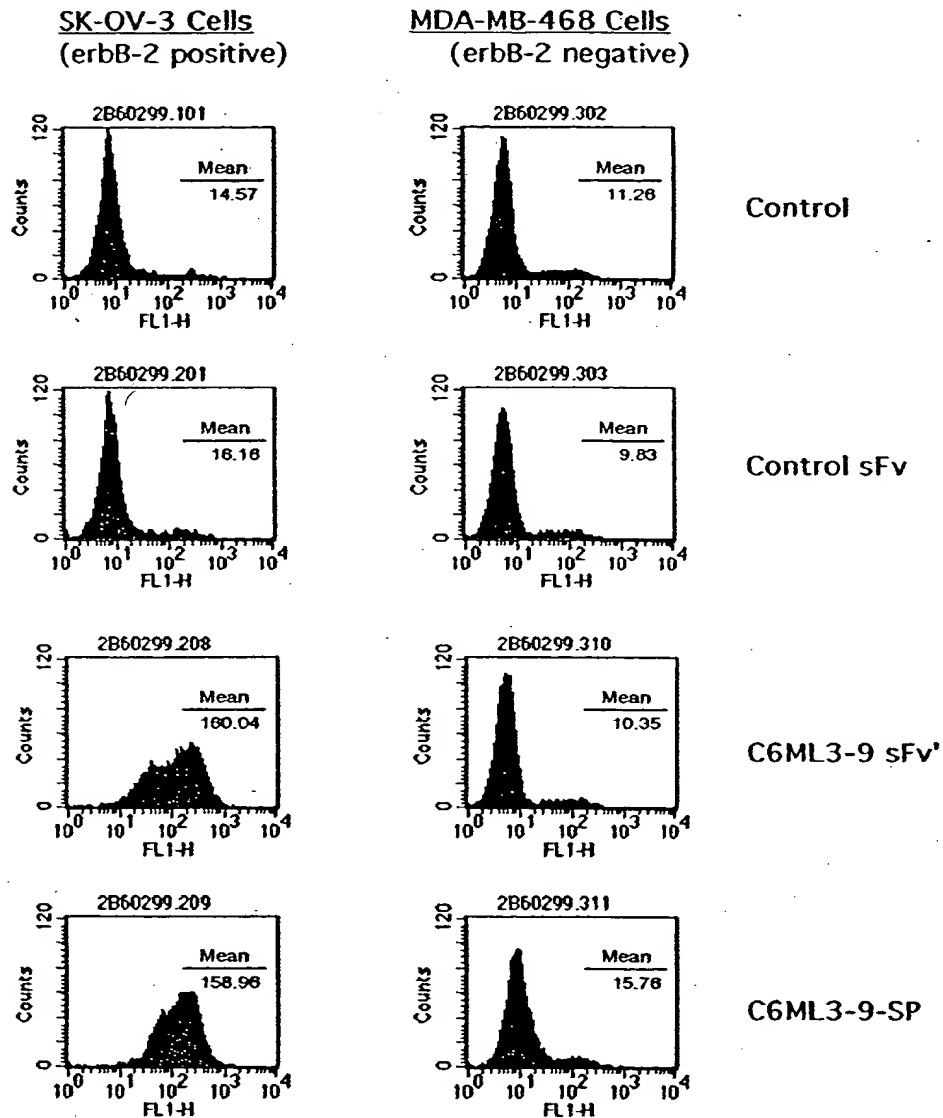
-QVQLVQSGAE VKKPGESLKI SCKGSGYSFT SYWIAWVRQM PGKGLEYMGL  
IYPGDSDTKY SPSFQGQVTI SVDKSVSTAY LQWSSLKPSD SAVYFCARHD  
VGYCSSSNCA KWPEYFQHWG QGTLVTVSSG GGGSGGGGSG  
GGGSQSVLTQ PPSVSAAPGQ KVTISCSGSS SNIGNNYVSW YQQLPGTAPK  
LLIYDHTNRP AGVPDRFSGS KSGTSASLAI SGFRSEDEAD YYCASWDYTL  
SGWVFGGGTK LTVLGAAAH HHHHGGGGCL ESSSSGSSSS  
GSTPPKKKRK V

## FIGURE 14

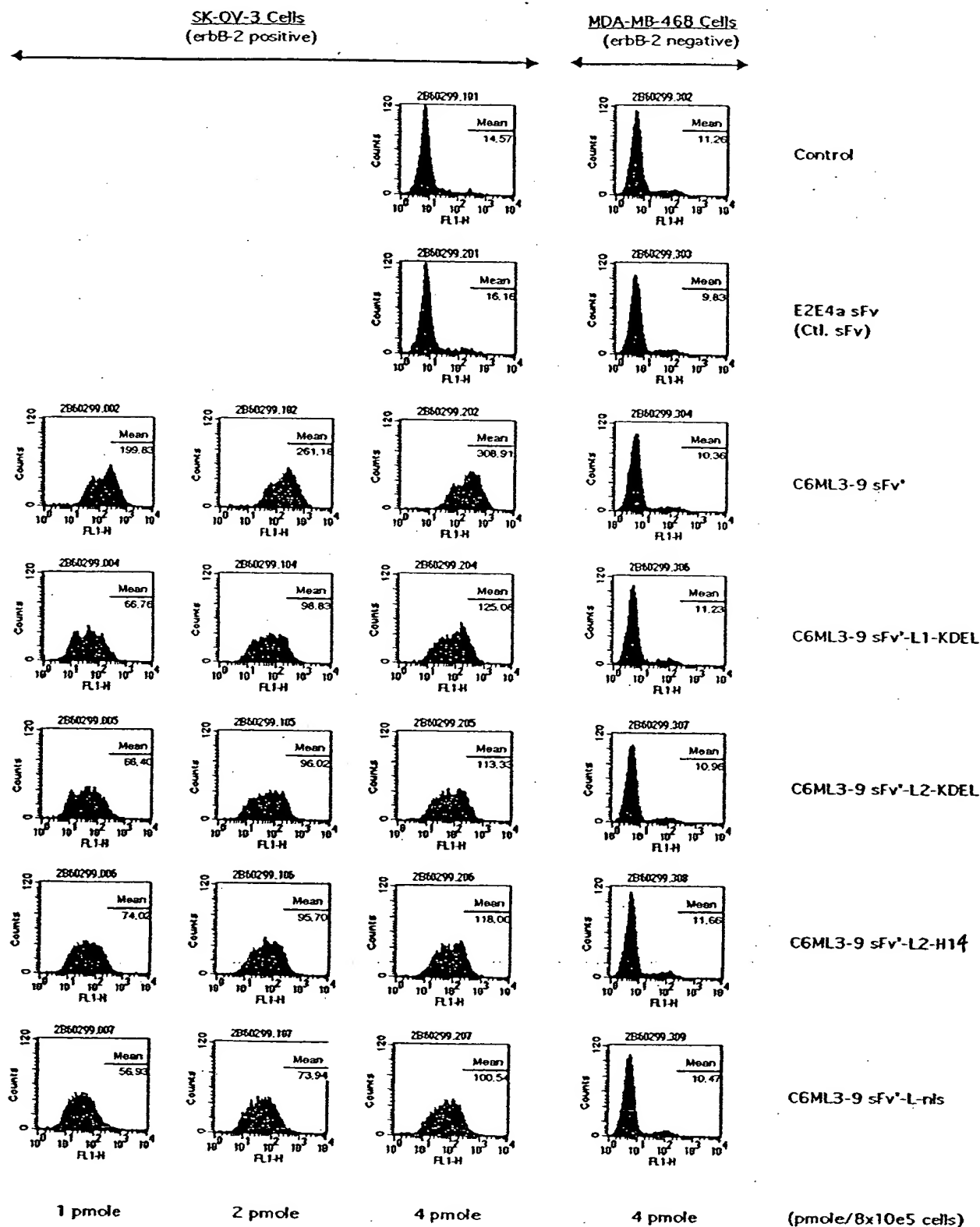
### C6ML3-9 sFv'-L2-nls NUCLEOTIDE SEQUENCE

5' caggtgcagctggtgcagctctggggcagaggtgaaaaagcccggggagtcctgaagatctcctgtaagggttctggata  
cagctttaccagctactggatcgcttgggtgcgccagatgccgggaaaggcctggagtacatggggctcatctatcctg  
gtgactctgacaccaaatacagcccgtcctccaaggccaggtcaccatctcagtcgacaagtcctgcagcactgcctac  
ttgcaatggagcagctctgaagccctcggacagcgccgtgtattttgtgcgagacatgacgtgggatattgcagtagttc  
caactgcgcaaagtggcctgaatacttcagcattggggccagggcaccctggtcaccgtctcctcaggtggaggcggtt  
caggcggaggtggctctggcgggtggcgatcgagctctgttgacgcagcgccctcagtgctctgcggccccaggacag  
aaggtcaccatctcctgctctggaagcagctccaacattgggaataattatgtatcctggtaccagcagctcccaggaa  
agccccaaactcctcatctatgatcacaccaatcgccccgaggggtccctgaccgattctctggctccaagtctggca  
cctcagcctccctggccatcagtggttccgggtccgaggatgaggctgattattactgtgctcctgggactacaccctc  
tcgggctgggtgttcggcgagggaaccaagctgaccgtcctaggtgcggccgcacaccatcatcaccatcacgggtggtg  
cggtgc ctcgagtcta gcagctccgg ttctctagc tctggatcca ctccgccgaa aaagaacgt aaagtg 3'

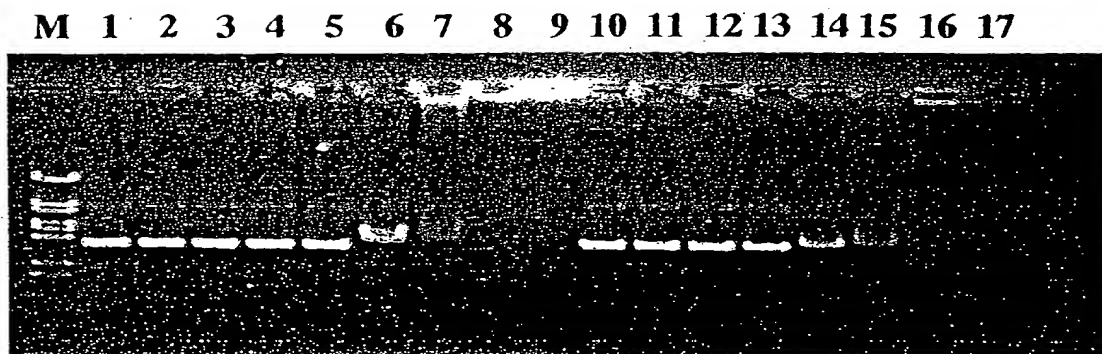
**Figure 15. C6ML3-9 sFv' and its salmon protamine conjugate binds specifically to the erbB-2 positive ovarian cancer cells**



**Figure 16. FACS Analysis of the erbB-2 Binding Activities of Bacterially Expressed C6ML3-9 sFv' and its Derivatives**



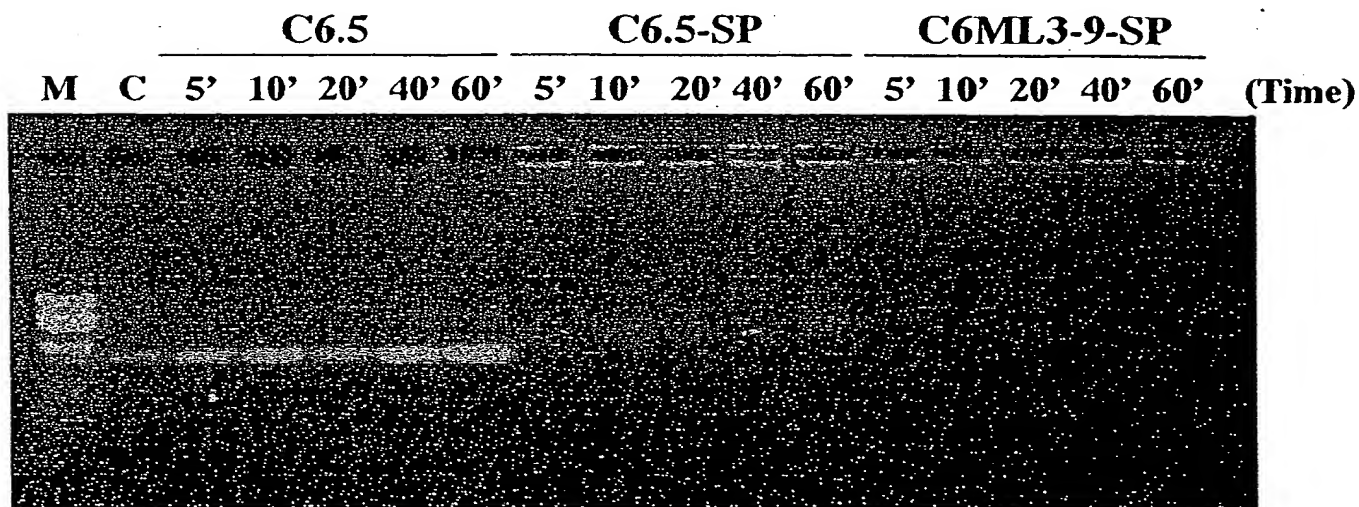
**Fig 17. Gel Shift Analysis of the C6.5-SP-DNA and C6ML3-9-SP-DNA Complex**



- M. DNA marker -  $\lambda$  DNA BstEII digest
1. 200 ng pGL3 DNA
  2. 200 ng pGL3 DNA + 1.45 pmol C6.5
  3. 200 ng pGL3 DNA + 2.90 pmol C6.5
  4. 200 ng pGL3 DNA + 5.80 pmol C6.5
  5. 200 ng pGL3 DNA + 11.6 pmol C6.5
  6. 200 ng pGL3 DNA + 1.45 pmol C6.5-SP
  7. 200 ng pGL3 DNA + 2.90 pmol C6.5-SP
  8. 200 ng pGL3 DNA + 5.80 pmol C6.5-SP
  9. 200 ng pGL3 DNA + 11.6 pmol C6.5-SP
  10. 200 ng pGL3 DNA + 1.45 pmol C6ML3-9
  11. 200 ng pGL3 DNA + 2.90 pmol C6ML3-9
  12. 200 ng pGL3 DNA + 5.80 pmol C6ML3-9
  13. 200 ng pGL3 DNA + 11.6 pmol C6ML3-9
  14. 200 ng pGL3 DNA + 1.45 pmol C6ML3-9-SP
  15. 200 ng pGL3 DNA + 2.90 pmol C6ML3-9-SP
  16. 200 ng pGL3 DNA + 5.80 pmol C6ML3-9-SP
  17. 200 ng pGL3 DNA + 11.6 pmol C6ML3-9-SP

\*0.8% agarose gel in 1xTAE, 150v, RT, ~1hr, EtBr staining overnight

**Figure 18. Kinetic Study of the C6.5-SP-DNA and C6ML3-9-SP-DNA Complex Formation**

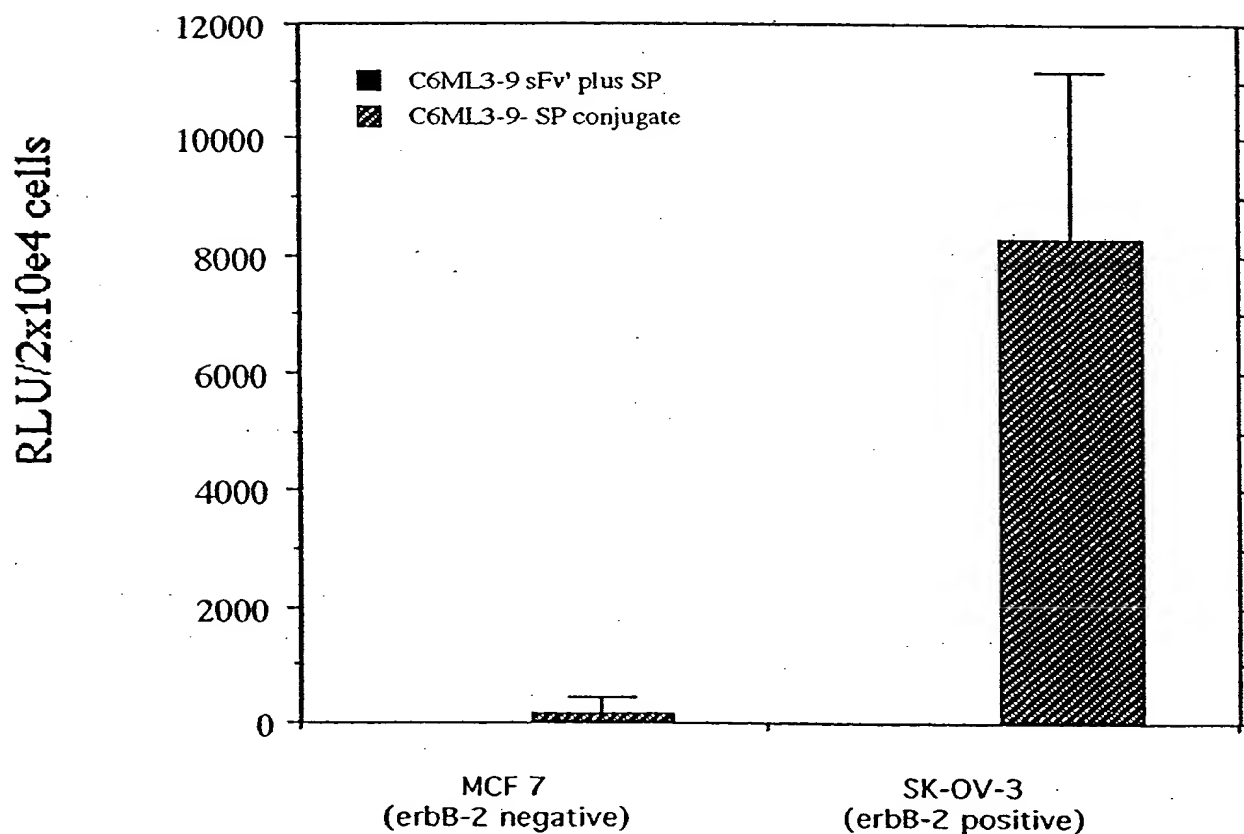


M. DNA marker -  $\lambda$  DNA BstEII digest

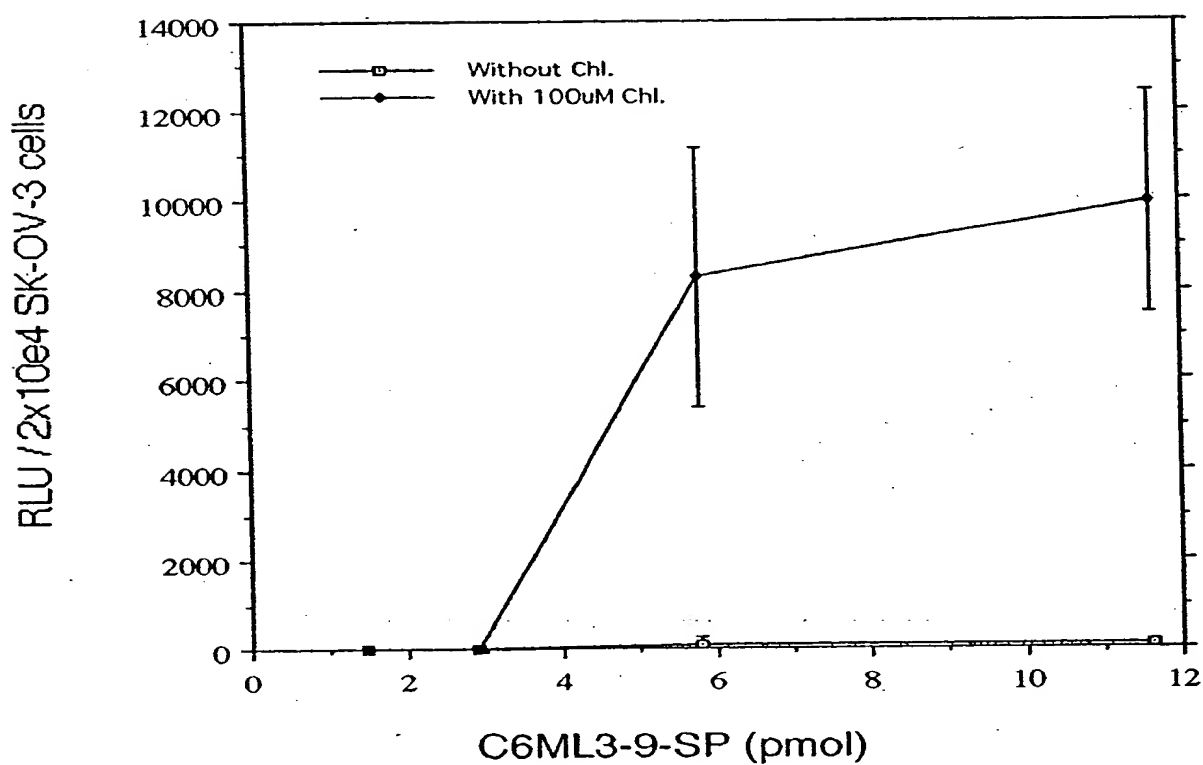
C. 200 ng pGL3 DNA alone

\* The rest of the lanes - 200 ng pGL3 DNA incubated with 5.8 pmol proteins as indicated above each line, on ice, for different period of time. Electrophoresis condition same as Figure 3.

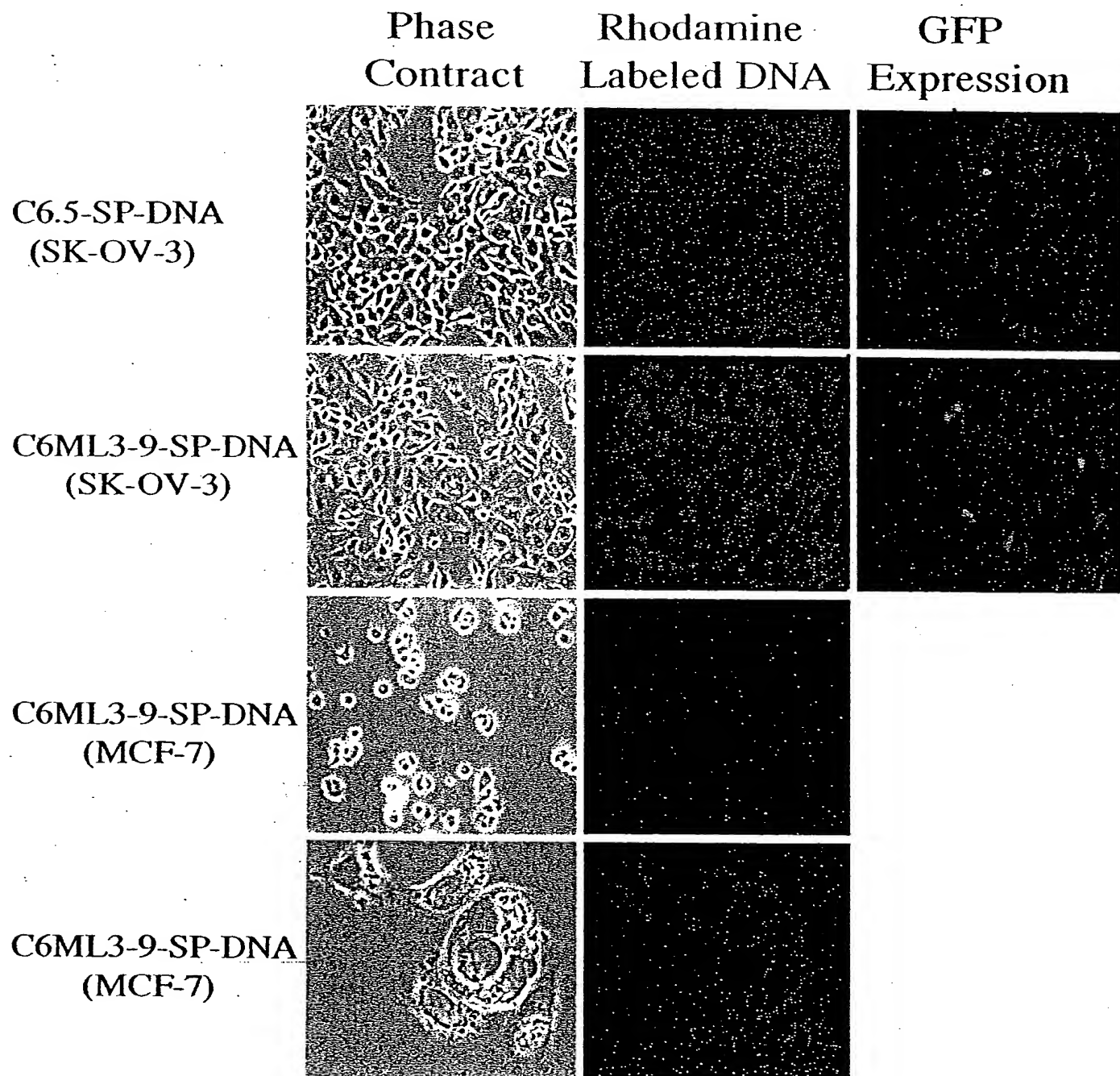
**Figure 19. The C6ML3-9-SP conjugate protein mediates specific luciferase gene delivery to erbB-2 positive cancer cells**



**Figure 20. Chloroquine-dependent C6ML3-9-SP-mediated Gene Delivery**



**Figure 21. Fluorescent microscopy of C6.5-SP and C6ML3-9-SP-mediated gene transfer of pGeneGrip Rhodamine/GFP plasmids with SK-OV-3 and MCF-7**

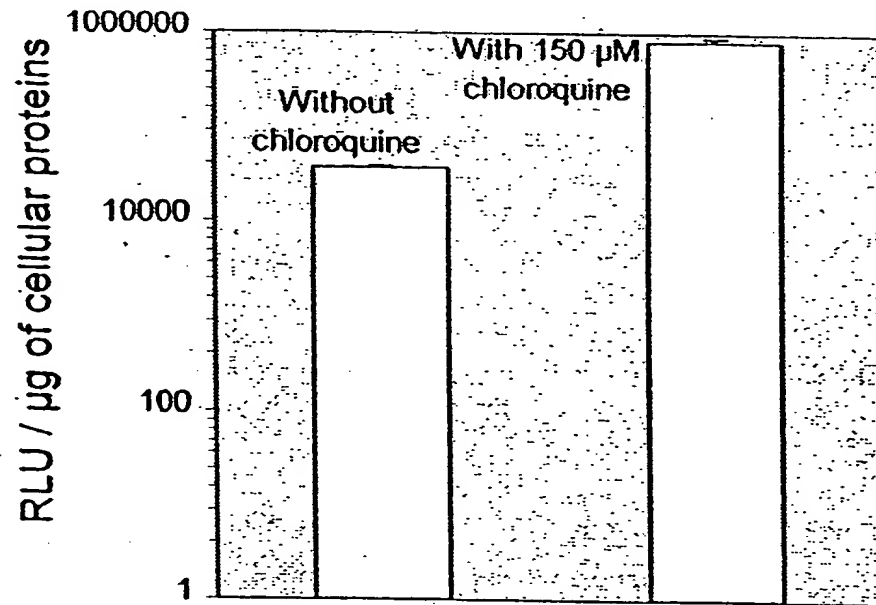


05688721.062501



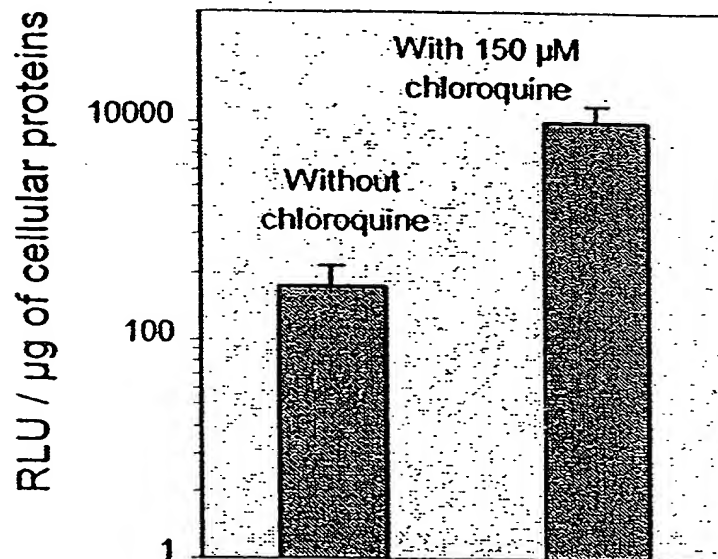
## FIGURE 22

### THE EFFECT OF CHLOROQUINE ON 3T3-HER2 TRANSFECTION MEDIATED BY C6ML3-9sFv'-SALMON PROTAMINE



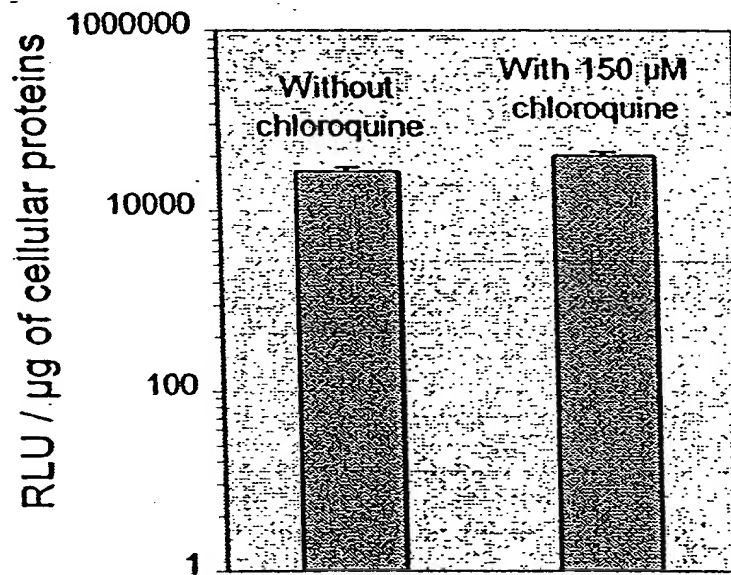
## FIGURE 23

### THE EFFECT OF CHLOROQUINE ON 3T3-HER2 TRANSFECTION MEDIATED BY C6ML3-9sFv'#2-P1



## FIGURE 24

THE EFFECT OF CHLOROQUINE ON 3T3-HER2  
TRANSFECTION MEDIATED BY C6ML3-9sFv'#2-H1



## FIGURE 25

THE EFFECT OF  
C6ML3-9sFv'-H1-pBks ON 3T3-HER2  
TRANSFECTION MEDIATED BY C6ML3-9sFv'-H1

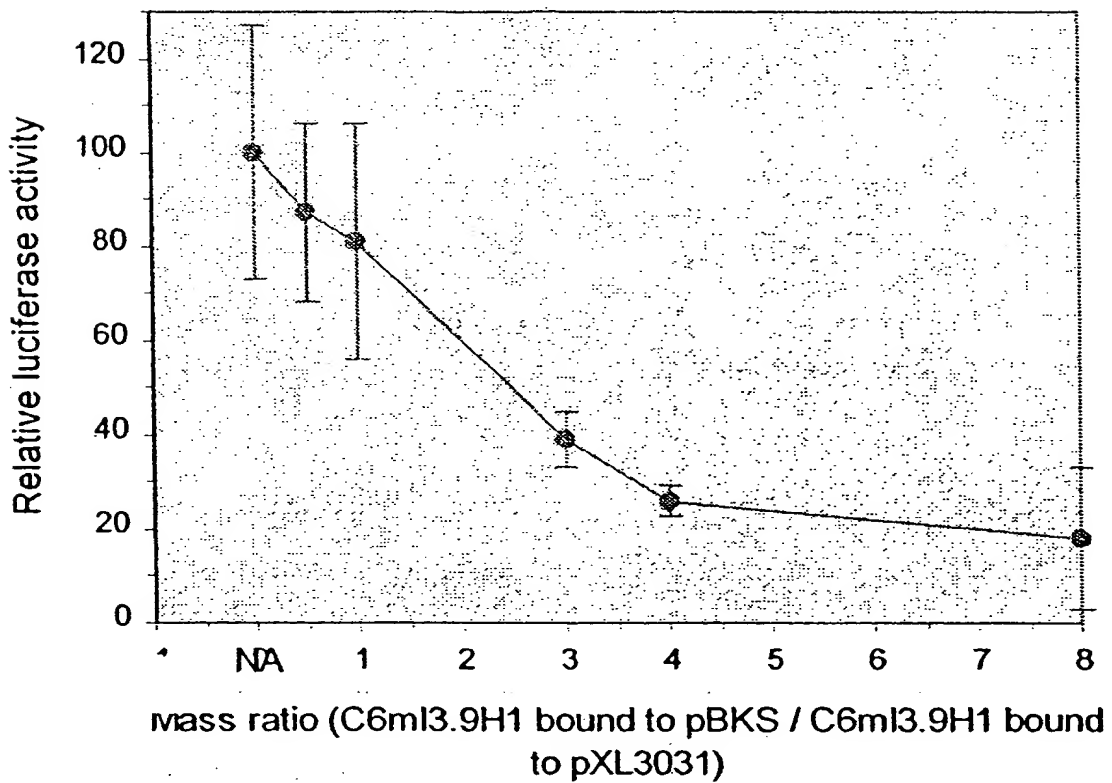


FIGURE 2

THE EFFECT OF THE DNA TO C6ML3-9sFv'-H1  
RATIO ON 3T3-HER2 TRANSFECTION EFFICIENCY

